An antibody against SSEA-5 glycan on human pluripotent stem cells enables removal of teratoma-forming cells.

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Authors: C Tang, A S Lee, J P Volkmer, D Sahoo, D Nag, A R Mosley, M A Inlay, R Ardehali, S L Chavez, R R Pera, B Behr, J C Wu, I L Weissman, M Drukker

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Public Summary:
One of the biggest risks to the clinical application of embryonic stem cell research is the risk of tumor formation. Such tumors, known as teratomas, form because there exists embryonic stem cells that have not completely become the desired transplantable tissue. These undifferentiated cells have rightfully become a cause of great concern and threaten to stop the clinical implementation of embryonic stem cells. We have developed an antibody against such cells that is able to recognize and thereby remove these cells before transplantation. We found that using this antibody alone drastically reduces the frequency of teratoma-forming cells. However, when this antibody is coupled with two other antibodies, which also target embryonic stem cells, we are able to achieve complete removal of all teratoma forming cells. This work holds great promise to facilitate the clinical utilization of embryonic stem cell based therapeutics.

Scientific Abstract:
An important risk in the clinical application of human pluripotent stem cells (hPSCs), including human embryonic and induced pluripotent stem cells (hESCs and hiPSCs), is teratoma formation by residual undifferentiated cells. We raised a monoclonal antibody against hESCs, designated anti-stage-specific embryonic antigen (SSEA)-5, which binds a previously unidentified antigen highly and specifically expressed on hPSCs-the H type-1 glycan. Separation based on SSEA-5 expression through fluorescence-activated cell sorting (FACS) greatly reduced teratoma-formation potential of heterogeneously differentiated cultures. To ensure complete removal of teratoma-forming cells, we identified additional pluripotency surface markers (PSMs) exhibiting a large dynamic expression range during differentiation: CD9, CD30, CD50, CD90 and CD200. Immunohistochemistry studies of human fetal tissues and bioinformatics analysis of a microarray database revealed that concurrent expression of these markers is both common and specific to hPSCs. Immunodepletion with antibodies against SSEA-5 and two additional PSMs completely removed teratoma-formation potential from incompletely differentiated hESC cultures.